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RADIUM

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A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES

RADIUM

A MONTHLY JOURNAL DEVOTED TO THE CHEMISTRY, PHYSICS AND THERAPEUTICS OF RADIUM AND RADIO-ACTIVE SUBSTANCES.

Edited and Published by Charles H. Viol, Ph. D. and William H. Cameron, M. D., with the assistance of collaborators working in the fields of Radiochemistry, Radioactivity and Radiumtherapy.

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VOL. IV JANUARY, 1915 No. 4

CLASSIFICATION OF THE VARIOUS METHODS EMPLOYED IN THE INTERNAL ADMINISTRATION OF RADIUM EMANATION AND RADIUM SALTS.

BY WILLIAM H. CAMERON, M. D., AND CHARLES H. VIOL, PH.D.

In this communication, it is our intention to suggest a classification for the various methods of employing radium emanation and radium salts in internal medicine. We believe that such a classification is necessary in order that the terminology of current literature on the subject may be generally understood. Furthermore, we hope to acquaint the medical profession at large, not only with the relative therapeutic value of the several methods, but the economic value as well.

One of us has had the opportunity of making a comparative study of the clinical results obtained by the use of most of the methods described and the other of us made a study of the physics and chemistry of the radioactive substances, the analytical methods of determining these and the mechanical principles underlying the economic application of radium emanation. Our conclusions, therefore, are based on a most careful study of the entire subject.

Before taking up our classification, something must be said about dosage and the terminology. The literature dealing with the use of radium salts, radium emanation and other radioactive substances in internal medicine is only less voluminous than that dealing with the local application of the rays of radium and mesothorium. Many units have been used to express concentrations of

radium emanation and quantities of radium salts. This led to uncertainty and confusion when these substances were used and it was recognized that there was a great need for an international standard and a better defined unit for expressing the concentration of radium emanation. As a result of the work of the Committee appointed by the Congress of Radiology and Electricity at the Brussells Meeting in 1910, Madame *Curie* in 1911 prepared a standard which was accepted in 1912 as the International Radium Standard. A prototype standard was also prepared and is kept at Vienna in the Institute for Radium Research of the Vienna Academy of Sciences. Standards which have been carefully compared with the International Standard and the Vienna Secondary Standard are now in the possession of different countries including the United States Bureau of Standards at Washington. At the above mentioned Congress, it was further decided to call the quantity of radium emanation which is in equilibrium with one gram of radium element—the "curie" in honor of M. and Mme. *Curie*. The curie is a very large unit and, for ordinary use, it is more convenient to express quantities of radium emanation in terms of the millicurie and microcurie, these being respectively one-thousandth and one-millionth of a curie and equal to the radium emanation in equilibrium with one milligram and one microgram of radium element. The mache unit, much used in the past in Germany and Austria to express concentrations of radium emanation, is a much smaller unit than the microcurie. One microcurie of radium emanation per liter equals a concentration of 2700 mache units.

On the basis of *Rutherford* and *Soddy's* "disintegration theory" the accumulation of radium emanation may be explained as follows: All the radioactive elements are disintegrating or transmuting at a rate that is definite and invariable for each radio-element. Thus, the time required for the disintegration of half of any quantity of radium is about 1750 years. For radium emanation the period of half decay is 3.85 days. In any given quantity of radium there are being produced every second a certain number of atoms of emanation due to disintegration of radium atoms, this number being a very small fraction (0.000,000,000,01) of the total number of radium atoms present. If the radium is initially freed from emanation atoms by any suitable means, there will be formed in the first second this same definite number of emanation atoms, and of these a certain proportion (0.000,002) will change in the next second into the next product, Radium A, but not all will change. In the second second, more emanation atoms are formed and since there are now these together with the emanation atoms remaining from the first second, the number of emanation atoms changing in the second second is greater, since it is always the same fraction of *all* the emanation atoms present (0.000,002). *In this way there is a piling up of the emanation atoms until the number of these changing per second equals the number produced per second from the radium. This limiting condition is called that of radioactive equilibrium.* In a sealed

radium preparation, this condition of radioactive equilibrium between the radium and the emanation is half attained in 3.85 days. It is approximately attained in a month. The following table shows the decay of radium emanation and the rate of accumulation of emanation in a sealed radium preparation:

A equals fraction of emanation remaining after time t.
B equals fraction of equilibrium amount of emanation formed in t days in a radium preparation initially free from emanation.

Time	A	B
0	1.0000	.0000
1 hr.	.9925	.0075
6 hrs.	.9560	.0440
12 hrs.	.9139	.0861
18 hrs.	.8737	.1263
1 day	.8353	.1647
2 days	.6977	.3023
3 days	.5827	.4173
4 days	.4868	.5132
5 days	.4066	.5934
6 days	.3396	.6604
7 days	.2837	.7163
8 days	.2369	.7631
9 days	.1979	.8021
10 days	.1653	.8347
12 days	.1153	.8847
14 days	.0805	.9195
16 days	.0561	.9439
18 days	.0392	.9608
20 days	.0273	.9727
25 days	.0111	.9889
30 days	.0045	.9955
40 days	.0007	.9993
50 days	.0001	.9999

One curie of emanation is the equilibrium amount of radium emanation produced by one gram of radium element.

Being a gas, the radium emanation when present in any preparation, has a great tendency to escape since the amount of emanation normally present in the air is an exceedingly small quantity. Some solids such as minerals and charcoal hold the emanation with considerable tenacity, but if the solid is finely divided and the air supply is sufficient, all the emanation will eventually be lost. Because of the ease with which emanation diffuses away from solutions, etc., it is always necessary to use great precautions to avoid such mechanical losses. So, for example, when a solution of radium emanation is being taken *per os,* it should be drunk through a tube from the original container. Again the emanation is not very soluble in water. In a closed vessel half filled with water, at ordinary temperature (20-25° C.), emanation would be so distributed that four-fifths would be in the air space and one-fifth dissolved in the water; that is, the concentration of the emanation in the water would be one-fourth the concentration of the emanation in the air above. For this reason, it is necessary to use all of any emanation preparation at one dose. If, for example, a bottle of emanation water were half emptied, at a dose, in a short time four-fifths of the remaining emanation would pass into the air space above and the second dose would contain only one-fifth as much emanation as did the first dose.

The radioactive decay of emanation is such that in 3.85 days, half of the remainder disintegrates, and so on, so that after a month practically all the emanation has decayed. Of course, if radium is present in the preparation the decay of the radium produces more emanation—but in any emanation preparation (such as most of the naturally active mineral waters) after one month, practically all of the emanation has disintegrated and the radioactivity of the water is almost nil.

The necessity of giving exact data in regard to the quantities of radium salt and concentrations of radium emanation employed cannot be too strongly emphasized. Unless such data (based on actual electroscopic measurement by reliable authority) is given when making the case reports, they lose value, since there is no possibility of comparing results with those of others who may or may not have worked under the same conditions. It should also be clearly stated which method has been employed.

Depending upon the radioactive substances used, there are, in internal medicine two main divisions recognized:

First,—Administration of radium emanation (Part A and B).

Second,—Administration of Radium Salts (Part C).

We will take up the consideration of the various methods of administering radium emanation, the dosage employed, and a short description of its properties.

Radium emanation is the disintegration product resulting after radium atoms have undergone a transmutation consisting in the emission of an alpha particle (ray). The alpha particles are positively charged helium atoms shot out with tremendous velocity (10,000 to 15,000 miles per second) from the parent atom. Radium emanation is a gas which is absolutely inert—chemically—forming no compounds. One curie of emanation gas has a volume of 0.6 cubic millimeters at O° C and a normal pressure of 760 mm. The weight of a curie of emanation is 0.006 milligrams. The heating effect, due to the alpha rays from one curie of emanation, amounts to 28.6 gram calories per hour.

In order to study the various methods, we herewith submit the following classification:

(Classification based on source of radioactivity).

PART A. Naturally occurring emanation.

- I. Inhalation.
  - room.
  - bath.
- II. Deglutition.
- III. Hypodermatic.
  - Intermuscular.
  - Intra-articular.
  - Intravenous.
- IV. Enema.

PART B. Artificially prepared emanation.

- I. Inhalation.
  - Room type.
    - With aid of oxygen or air.
  - Individual type.
    - With aid of oxygen or air and electricity.
  - Bath

II. Deglutition.

III. Hypodermatic. { Intermuscular. Intra-articular. Intravenous.

IV. Enema.

Part A.

THE ADMINISTRATION OF NATURALLY OCCURING EMANATION—ROOM INHALATION.—This method consists in placing patients in an air-tight room or compartment, into which, or through which, a stream of natural radioactive water is flowing. The concentration is influenced by the amount of emanation taken up by the water in its course through some deposit of radioactive material in the depth of the earth, and by the rate by which the emanation is given off after it reaches the room or compartment. The only exact method by which the concentration of emanation in the room can be determined is by electroscopic analysis of the room air at the time of treatment. An approximate dose can be estimated by a knowledge of the average daily concentration of the water, the accumulated daily concentration in the room and the air capacity. The dosage should be expressed in terms of microcuries per liter of air.

Because of the uncertainty in the determination of the dosage, the difficulty of adjusting same to the individual case, and on account of the inadequate concentration of most waters* we believe this method, used alone, is therapeutically inadequate and that cases so treated should not be considered in compiling statistics. This fact is now generally recognized as most places using such methods augment the cencentration by artificial means or by administering large quantities of natural radioactive water.

ADMINISTRATION OF NATURALLY OCCURING EMANATION—NATURAL RADIOACTIVE BATH.—There is considerable dispute among workers abroad as to the power of radium emanation to penetrate the skin. We believe that very little, if any, absorption actually takes place in this manner and that the therapeutic effect is derived entirely from the inhalation of the emanation as it comes from the water. Such being the case, opportunity should be given the patient to inhale all the emanation possible. This can be controlled to some extent by erecting a tent over the tub. Unless the natural radioactive water used is of a suitable temperature for a more or less prolonged immersion, considerable emanation will be lost in the process of heating. The higher the temperature the more rapidly will the emanation be given off and this factor must be considered in working out a technic for the individual case.

(*See *Lazarus.* Radium Biologie und Therapie, pages 195-201, for concentration of natural springs abroad. Data with regard to springs in the United States is very meagre, and none of the springs so far examined have shown any notably high concentration of radium emanation.)

The most exact method of determining the dose used is by an analysis of the air confined in the air space at time of treatment. An approximate dose can be determined by a knowledge of the emanation concentration of the water. The dosage should be expressed in terms of microcuries of emanation per liter of water in tub or per liter of confined air above the water line.

If sufficient concentration (in our opinion not less than 0.05 microcuries per liter) is present in the natural water, this method has some advantage in that it combines the eliminating and quieting effect of a continuous warm bath with emanation. What has been said as to the therapeutic value of the inhalation of naturally occuring emanation when used alone also applied to the method just described.

ADMINISTRATION OF RADIUM EMANATION—DEGLUTITION.—The only economical method of getting naturally occurring radium emanation into the stomach is in the form of naturally occuring radioactive water. By reason of the fact that it can be taken at frequent intervals, it is also the most effective single method of administering naturally occurring emanation. It is unfortunate that the decay is so rapid (half period being 3.8 days) that it is not practical to use naturally occurring radium emanation water any great distance from the source of supply. If the water originally contained 1 microcurie, at the end of four days it will contain ½ microcurie; and at the end of eight days ¼ microcurie, and at the end of thirty days practically all radioactivity will have disappeared. *Hence natural radioactive waters can never be used for general distribution.*

There are only a few natural springs in the world of sufficient dosage to give a true therapeutic effect and when results are obtained, except in the mildest type of cases, it is perhaps due to the continued effect which comes from frequently repeated doses. The original emanation concentration can be accurately determined by electroscopic methods and if the rate of decay is properly calculated, the dose of any single quantity can be determined at any period before consumption. The dosage should be expressed as microcuries or millicuries per liter.

ADMINISTRATION OF NATURALLY OCCURRING RADIUM EMANATION—HYPODERMATICALLY.—The intermuscular, intra-articular and intravenous injection of naturally occurring radium emanation, in the form of naturally occurring radium emanation water, is practically worthless from a therapeutic standpoint, as it is difficult to properly sterilize such a solution without a great loss of the emanation and the dosage is too low.

ADMINISTRATION OF NATURALLY OCCURRING RADIUM EMANATION WATER—ENEMA.—Because of the slight activity of most natural waters, this method of application is of no vlaue; in fact, the last two mentioned methods are included in our classification simply because they have been, at times, advocated and we desire to place them in their proper light.

Part B.

ADMINISTRATION OF ARTIFICIALLY PRODUCED RADIUM EMANATION—INHALATION, ROOM-TYPE.—This method consists in conveying the emanation produced by a soluble radium salt in solution by means of an oxygen stream or compressed air into an air tight room or compartment. Oxygen is not only used to convey the emanation, but to replace the oxygen which has been used up in breathing. It is more economical, however, to use air under pressure for this purpose, in which case some arrangement should be made for pumping the air out of the room, washing out the excess carbon dioxide and returning the air without loss of emanation.

The available dose for each patient can be estimated from the known amount of radium element in solution and the air capacity of the room. The exact dosage available can be determined by an electroscopic examination of the room air for emanation at the time of treatment.

This method has the disadvantage of confining a number of persons in a closed room, the carbon dioxide content of which is considerably above the normal; the possibility of bacteriacidal contamination; the difficulty of individual dosage; and, due to the short length of time it takes for the blood to lose the emanation after the patient has passed out of the room, the treatment can only be effective if applied intensively.

In our experimental work with this method, we used, on human beings, the emanation produced by 2 to 74 milligrams radium element, giving a room concentration of from 0.003 to 0.8 microcuries per liter of air (3 to 2100 mache units). On animals, we succeeded in securing a lethal dose by the use of a concentration of 2600 microcuries per liter of air (70,000,000 mache units).

The results obtained from low concentrations of emanation were practically nil and it is best that about 25 milligrams of radium element should be employed in this work. It was demonstrated, by examination of the blood of patients for emanation, that in three hours practically all the emanation had disappeared. Therefore, treatment by this method always should be augmented by additional emanation given in the form of emanation solutions per os.

ADMINISTRATION OF ARTIFICIALLY PRODUCED RADIUM EMANATION—INHALATION, INDIVIDUAL TYPE.—In this method, the emanation instead of being set free in a room is carried to an individual inhalation apparatus placed over the patient's mouth and nose. The multiple type (for treating more than one patient at a time) has the advantage of permitting patients to sit or lounge in a well lighted and well ventilated room and an arrangement can be had which allows better regulations of dosage for the individual case. The one or two patient type can be made portable and has the advantage of being able to use a less amount of radium element to secure the same individual concentration. It can be used also in hospital work for bedfast patients, in which case the available concentration can be augmented by erecting a tent on the patient's bed.

Recently an effort has been made to use electricity for augmenting the concentration, the idea being to have the patient (nude) sit in a cabinet having the negative pole attached to some part of the body. We are of the opinion that this method offers little, since the active deposit is only deposited on the skin, where it would have but slight effect. What has been said of the room type emanator regarding the estimation of dosage applies also to the individual type.

Administration of Artificially Produced Emanation—Inhalation, Radioactive Bath.—This form of administration of emanation consists in rendering the bath water radioactive by taking the emanation from a soluble radium salt in solution. It has the advantage over the natural radioactive water in that it can be made any concentration desired, depending, of course on the amount of radium element. What we have described under the natural bath water as to estimation of dosage and technic also applies to this method.

Administration of Artificially Produced Emanation—Deglutition.—Many substances are capable of being rendered radioactive, but, on account of the rapid decay of the emanation, the only practical and economical method of administering is in the form of radioactive water. The method of production is simple and does not require an elaborate equipment. It consists in conveying the emanation, produced by a soluble radium salt in solution, into a container filled with distilled water. As the emanation is also soluble, the concentration in the distilled water is in direct proportion to the amount of radium contained in the soluble salt. Like the natural waters, artificially produced emanation water is not a permanently radioactive solution and, therefore, it is not a practical commercial possibility, except where it can be delivered fresh every day. It has a decided advantage over naturally occurring water, in that the concentration can be made any strength desired, and when used in sufficient dosage at frequent intervals, is the most effective single method of administering emanation products.

We have used on human beings, emanation solutions containing from 1 to 10,000 microcuries (2700 to 27,000,000 mache units), our maximum dose being by far the largest dose ever attempted. We consider a dose with an original emanation concentration of less than 1 to 2 microcuries as insufficient, and an average daily dose of radium emanation should be 10 to 20 microcuries (27,000 to 54,000 mache units). A fair dose would be from 14 to 21 microcuries. In this connection, it is well to mention the fact that the Radium Institute of London administers 250 to 500 microcuries of emanation as the daily dose.

Recently numerous machines have been put on the market for the production of radioactive water. The principle of these machines is the enclosing of an insoluble radium salt in a porcelain or other pervious capsule or rod, the idea being to have the emanation escape into the water in which the radium container is immersed. Considering the fact that the amount of emanation

actually able to pass out would be only from two to ten per cent of the amount produced by the radium contained, we do not believe, from an economic standpoint, that this method is practical, since very large amounts of radium element must be used in order to secure sufficient dosage, thus making this form of treatment almost prohibitive from the standpoint of cost.

ADMINISTRATION OF ARTIFICIALLY PRODUCED RADIUM EMANATION—HYPODERMATICALLY.—The preparation of a solution for intra-articular, intermuscular or intravenous injection in this way is possible because distilled water or normal physiological salt solution can be used in the preparation of same. To secure sufficient dosage, the emanation from a large amount of radium is necessary. For practical purposes, therefore, this form of using emanation is not generally available.

ADMINISTRATION OF ARTIFICIALLY PRODUCED RADIUM EMANATION—ENEMA.—A solution for use as an enema can be prepared as described in the preparation of emanation solutions for drinking purposes. The water cannot be redistilled or sterilized without loss of emanation. As the emanation would not be taken up so rapidly, it would be necessary, then, to have a large concentration in order to secure a physiological effect.

Part C.

INTERNAL ADMINISTRATION OF RADIUM SALTS.

(a) Deglutition.
- Drinking solution.
- Tablets, Pills, Capsules, etc.

(b) Hypodermatic
- Intermuscular.
- Intra-articular.
- Intravenous.

(c) Bathing solution.

(d) Enema.

GENERAL CONSIDERATIONS.—Perhaps the first attempt toward the internal administration of radium element was made by M. *Jaboin* and M. *Beaudoin* who, according to the formula of *Rutherford,* incorporated 1-10 microgram of radium bromide in 10 liters of natural radioactive water for the purpose of making a permanently radioactive solution. In 1906, *Wickham* and *Degrais* first injected soluble radium salts and after injecting some thirty patients (doses from 1 to 10 micrograms per cc.) conclude that the body can bear perfectly certain doses of radium. They further state that the urine was radioactive for three or four days following the injection and that this radioactivity decreased steadily during the next four days in accordance with the laws of decrease of induced radioactivity. M. *Dominici* and M. *Faure Beaulieu* have shown that the injection of an insoluble radium salt is arrested in living tissue and may remain at least sixty-seven days. M. *Chevrier,* M. *Renon* and M. L. *Marie* also studied the effect of such injection. *Wickham* and *Degrais,* in their report to the Congress on Physico-Therapy conclude as follows:

"Subcutaneous, intravenous, intrapulmonary, intraperitoneal, intrapleural and subarchoid injections of radium sulphate are harmless; even in infants there is, during the first two hours after injection, only a slight and transient state of cardiac depression or stimulation."

In co-operation with Doctor Frederick *Proescher* and others, we have carried on extensive experiments with the use of radium element internally, using from 1 to 10 micrograms in 60 cc. of water by mouth and from 10 micrograms to one milligram in 2 cc. of normal physiological salt solution, given intravenously. As far as we are able to learn, this has been the most extensive work carried out in internal administration of radium. Even with the use of 1 milligram doses, we have, up to this time, never seen the slightest ill effect, the only contra-indication noted being an extremely low blood pressure.

The following table shows the distribution of radium salts following an intravenous injection of one milligram radium element in the form of a soluble salt. It is to be noted that by far the largest percentage is recovered from the bone and bone marrow, where it is deposited as an insoluble salt. It is to be noted further that the carcinomatous tissue present in this particular case does not show an excessive percentage of radium.

One Milligram Radium Element Injected, September 1, 1913.

Diagnosis—Cancer of Uterus.

Autopsy held—December 17, 1913.

No.	Part	Wet Weight.	Dry Weight.	Radium in Sample.	Radium Per Gram Dry Weigth
1.	Heart tissue ..	11.7 gm.	2.26 gm.	.000118 micrograms	0.00005
2.	Aorta tissue abdominal ...	13.4 "	2.79 "	.00219 "	0.00080
3.	Bone marrow (sternum) ...	20.5 "	7.01 "	.04414 "	0.00630
4.	Liver	11.9 "	2.48 "	.01530 "	0.00610
5.	Suprarenal capsule	5.3 "	0.91 "	.000118 "	0.00013
6.	Carcinomatous tissue mass of the parametrium	12.4 "	2.17 "	.000275 "	0.00012
7.	Para thyroid gland	0.12 "	0.035 "	Trace? "	.....
8.	Bone marrow lumbar region	9.18 "	3.73 "	.01780 "	0.00480
9.	Intestines	17.7 "	5.10 "	.000700 "	0.00014
10.	Thyroid gland..	13.3 "	2.74 "	.000700 "	0.00026
11.	Kidney	15.0 "	3.41 "	.000090 "	0.00003
12.	Stomach	15.5 "	3.30 "	Trace?	.....
13.	Lung	4.77 "	0.82 "	.00163 "	0.00200
14.	Pancreas	7.12 "	1.38 "	.00059 "	0.00043
15.	Spleen	11.83 "	2.90 "	.00196 "	0.00067
16.	Retroperitoneal gland	26.6 "	11.80 "	.00141 "	0.00013

INTERNAL ADMINISTRATION OF RADIUM SALTS—DEGLUTITION, DRINKING SOLUTION.—By dissolving soluble radium salts in redistilled water and permitting the solution to stand thirty days, or, until the contained salt has produced its equilibrium amount of emanation, a permanent radioactive solution is prepared. To prevent undue loss of the accumulated emanation, the solution should not be greater than an amount which can be administered at one dose, and should contain enough radium element per dose to give a daily dose of not less than 4 microcuries (or 11,000 mache units). As will be seen later, this is the most economical method of admin-

istering radium salts by mouth. It not only has the advantage over emanation water by being permanent and, therefore, practical, but it represents definite dosage and will, by reason of the retention for a greater or less period of the radium salts in the stomach and intestinal tract, give a more prolonged therapeutic effect.

The dosage can be accurately determined by the electroscope and should be expressed in micrograms of radium element per dose.

INTERNAL ADMINISTRATION OF RADIUM SALTS—DEGLUTITION, —TABLETS, PILLS, CAPSULES, ETC.—Many substances such as charcoal, can be rendered radioactive temporarily by the use of radium emanation; permanently so, by incorporating with the substance radium element. The period of the activity produced by the emanation is so short that tablets, pills, capsules, etc., made by this process are absolutely worthless. It would seem, however, that radium element administered in this way would present many advantages. On the contrary, we condemn their use because the emanation which is produced by the contained radium element would necessarily have to be large in order to secure sufficient dosage. When administering radium salts in this manner the dosage should be expressed in micrograms of radium element per dose and it should be clearly stated in what form administered.

INTERNAL ADMINISTRATION OF RADIUM SALTS—HYPODERMATICALLY.—The only practical method of preparing solutions for intermuscular intra-articular or intravenous injections is by the use of a soluble radium salt, for by this method permanent and absolutely sterile preparations can be obtained, and, furthermore, exactness in dosage is assured. As before stated, we experimented with dosages ranging from 5 micrograms to 1 milligram put up in ampulles containing 2 cc. of physiological salt solution. At the present time, we consider a single dose of from 50 to 100 micrograms as therapeutically correct and absolutely safe. This amount can be repeated every 10 days, until the patient has received 300 micrograms. A larger accumulative dose, we consider not necessary for ordinary work. Our experimental work with the intermuscular and intra-articular injection was not extensive as our knowledge of the physical chemical and bacteriacidal powers of radium as applied in therapeutics, urged us to place it in the blood stream by the shortest possible route. In other words, we felt that the maximum effect of radium administered internally was obtained when it was injected intravenously, the blood stream at once carrying the radium to all parts of the system.

INTERNAL ADMINISTRATION OF RADIUM SALTS—BATHING SOLUTION.—Bathing solution must, of course, be permanent and can only be made so by the addition of soluble radium salts. Individual bath stock solutions should contain enough radium element which, when mixed with the bath water, will give a concentration of from 1 to 10 microcuries. Strictly speaking, this form of administration is by inhalation, and is only mentioned here because

soluble radium salts should be used in the preparation of the stock solutions. As a matter of fact, this form of radioactive bath is the only one in which an established dose can be satisfactorily administered. What has already been said regarding the technic of a radioactive bath also applies to this method. The dose should be stated as so much radium element per liter of bath water. The temperature of the water and duration of bath should be mentioned. Mention should also be made as to the open or closed (tent erected over tub) method.

INTERNAL ADMINISTRATION OF RADIUM SALTS—ENEMA.—We are not prepared to give an opinion as to the comparative therapeutic value of this method, as we considered that the accumulated emanation in the stock solutions would be entirely lost during the process of preparation for administration. The stock solution, should be put into a container that will permit heating of the fluid to at least 100° F. while still under seal. The container should then be connected directly to the rectal tube. Such a method may prove of value provided that the solution contains not less than four micrograms of radium element per dose.

In conclusion, we again desire to call the attention of physicians to the necessity of stating the correct dosage and to warn them that they must be absolutely sure that they are using preparations, the emanation concentration or radium element content of which cannot be questioned. All pharmaceutical radium preparations should be viewed with distrust if the radium content of the preparation is not specifically stated and guaranteed.

THE INFLUENCE OF RADIOACTIVE EARTH ON PLANT GROWTH AND CROP PRODUCTION.*

BY H. H. RUSBY, M. D.,

Dean of the College of Pharmacy, Columbia University.

The energy changes which take place in the disintegration of radioactive atoms are hundreds of thousands times greater than are the energy changes associated with ordinary chemical reactions, such as the burning of coal—one of our chief sources of energy. One gram of radium element gives off as much energy in its complete disintegration as is obtained in the burning of a ton of coal. However, the energy evolved by radioactive change is only available as the radio-elements transmute, and in the case of radium, this process is so slow that about 2,000 years are required for half of a quantity of radium to disintegrate, and only in 20,000 years is the change nearly complete. So far it has not been possible to alter the rate of transformation of the radio elements, and so these large stores of subatomic energy are continuously available in rather tiny quantities. Therefore the energy

*A lecture delivered at the New York Botanical Garden, November 14, 1914.

must be utilized with a view to obtaining results which are not to be obtained by the ordinary forms of energy such as heat, light and electricity.

Radioactive elements are continuously sending out so-called "rays" which have been found to fall into three groups. The readily absorbed rays (alpha rays) are material in nature—being positively charged helium atoms—which are shot out from the disintegrating radio elements with the tremendous velocity of 10,000 to 15,000 miles per second. Because of the friction which they meet in passing through a gas or a thin sheet of solid material, the alpha rays soon lose their high velocity, and are then ordinary helium gas atoms. In other words, the alpha rays are easily stopped or absorbed. The beta rays are particles of negative electricity which are shot out with nearly the velocity of light (186,000 miles per second) and because of their smallness they are able to penetrate rather considerable thicknesses of matter. The third type of rays is the most penetrating radiation that we know—since the gamma rays are able to penetrate considerable thicknesses of every substance. In order to completely absorb the gamma rays, the radium must be screened with more than a four-inch thickness of lead, or six inches of steel. Gamma rays are analogous to the X-rays, both being exceedingly penetrating forms of radiation, similar to ultra-violet light, but with a very much shorter wave length.

When the radium atom transmutes, it shoots out an alpha ray—and the remainder of the radium atom now constitutes a new element—radium emanation. Radium emanation is a gaseous substance which, like its parent substance radium, is also radioactive. Having the properties of a gas—radium emanation can diffuse, dissolve in liquids and solids. In the course of its radioactive decay the emanation gives rise to other radioactive products which are solids. Substances exposed to radium emanation become coated with the solid radioactive deposit which the emanation produces, and so may seem to be temporarily radioactive.

Radium is transmuting very slowly, as has been said, requiring about 2,000 years for the decay of half. The emanation changes much more rapidly, having a period of half decay of about 4 days. Thus any quantity of emanation will be half transformed in about 4 days. In the next 4 days, half of the remainder will transform, and so on, so that in about a month practically all of any emanation has disintegrated.

All of the radioactive substances are recognized as distinct chemical elements. Thus the only relation between radium and radium emanation lies in the production of the latter from the former. Chemically and physically they are wholly unlike, since radium is chemically a metallic substance similar to the metal barium, while the emanation is a chemically inert gas. Radium is not used in the form of pure radium metal, but in the form of the radium salts—the bromide, chloride and sulfate being most frequently used.

Radium bromide or chloride dissolved in water produces a radioactive solution that is quite permanent because of the slow decay of the radium. Radium emanation dissolved in water produces a radioactive solution that is only temporarily radioactive —since no matter what is done—the emanation undergoes its radioactive change—and in the course of a month—almost completely disappears. Most natural waters contain only radium emanation, and some of the springs at the celebrated watering places in this country and abroad contain quite notable quantities of the emanation.

The practical application of radium that is best known is in the alleviation, and in a great number of cases, the cure of cancerous affections. There are many other equally important medical uses for the substance, some already established, and others no doubt yet to be adopted. Just how radium acts upon the body and on malignant and other growths in producing its results is but imperfectly known, but it is certain of these phenomena first suggested the probability that radium would increase crop production in agriculture. It was early observed that while the application of a large amount of radium could kill cancerous growths, a shorter application might simply stimulate the growth. It was also found that this same difference between the effects of small and great doses of the rays on cancer exist in the case of healthy tissues, so as to render the careless handling of concentrated radium preparations extremely dangerous.

Since the general nature of living animal and vegetable protoplasm is identical, the question of influencing plant growth by the action of radium was at once suggested. Could it be applied to field crops so as to produce an increased yield? Could it be applied to crops suffering from animal or vegetable parasites, so as to kill the latter, as it affects cancer in man? Or, would the crops suffer more from such an application than would their diseases? If the application were found beneficial, would the amount of radium required for the purpose render the operation unprofitable? Or, knowing that the activity of a particle of radium goes on for centuries with no apparent diminution, would a single application permanently increase the agricultural productivity of the soil?

Plant physiologists, all over the world, took up investigations bearing on these questions. As would naturally be expected, these early investigations were restricted to experiments in laboratories, greenhouses, and gardens. In Europe, something has been done in experiments with field crops and orchards, but in this country no reports of extensive field trials have heretofore been made.

In October, 1913, I arranged with the Standard Chemical Company of Pittsburgh, Pennsylvania, to make preliminary trials on an extensive scale. In view of the cost of radium and its preparations, the reader may wonder how such an experiment could be undertaken. It requires about 400 tons of carnotite ore of standard quality to yield a gram (about 1-30th ounce) of radium, an amount

that could easily be carried on a man's thumb nail. The market price is $120,000 a gram or equal to $3,400,000 an ounce avoirdupois. This problem was solved by making use of the finely powdered residue which remains after all the radium possible has been extracted. This material contains some two or three milligrams to the ton, worth about $300, yet a by-product unless a special use for it could be discovered. Various other substances, especially uranium, are present in the material.

That the application of such material to the soil is a profitable procedure for the gardener or farmer may be understood when it is seen that such increases in production resulted as 29 per cent. in lettuce, 17 per cent. in lima beans, 35 per cent. in cucumbers, 35 per cent. to 44 per cent. in different varieties of squash, 80 per cent. in Rocky Ford muskmelons, 24 per cent. in carrots, 50 per cent. in sweet corn, and 70 per cent. in radishes, and that nearly all vegetables are much improved in their qualities. Lawns are benefited to an equal extent, and the size and brilliancy of garden and hot-house flowers is remarkably increased.

Before proceeding to describe these experiments and their results, it is desirable to briefly summarize the results of previous experimental work.

The most extensive work that has been published in English of the influence of radium on the growth of plants is that of Dr. Charles Stuart *Gager,* of Brooklyn, N. Y., which appeared in the fourth volume of the Memoirs of the New York Botannical Garden, December 2nd, 1908. Nearly all the authors quoted by Dr. *Gager* had reported that the effects of radium was to retard or inhibit plant development, results which, as it will be here shown, were due to the use of excessive quantities of radium. *Guilleminot* had especially commented on the difference between the effects of low and high activities. He stated that while a certain low activity had no effect upon plants, the effects of from six to twelve times that amount would markedly retard growth, and from eighteen to seventy-two times would completely destroy. Yet he expressed the opinion that there was no strength that would possibly stimulate growth. It was said that the distance at which the radium would act was limited to about two centimeters, less than an inch. Roots were found to be more susceptible than other parts of the plant. Some plants were more resistant than others and the turnip was mentioned as being especially so. Excessive branching of certain tissues was reported. It was found that parts of plants exposed to radium emanation would themselves become radioactive. The degrees of such radioactivity were, the root most, then, in order, stems, buds, leaves, and flowers. It was decided that this activity did not exist in the tissues themselves but in their contained water.

Gager himself employed numerous methods of experimentation. He used tubes of glass and other substances which were coated on the inside with substances containing radium. He also used rods similarly coated on the outside. Such tubes or rods would be laid upon dry seeds for various periods of time and the seeds were then planted and their germination and growth com-

pared with others not so treated. Seeds were soaked in water containing the emanation and were then planted and similarly compared. Plants were grown in water containing the emanations, while others, growing in the soil, were watered with such water. Plants were grown under bell jars in air that was kept charged with the emanation. Radium tubes and rods were buried in the soil in which seeds were planted. The radioactivities to which the seeds and plants were subjected in these experiments varied from 7,000 X up to 1,500,000 X, all of which we now know were excessive quantities of radium. He always found the damage greater with increase of activity. Similarly, he found that the seeds farthest away from the buried tube showed successively less injury. In short, it is seen that in every case of a change of conditions which resulted in a lower activity being exerted upon the seed or plant, the damage was less and he found strengths that would markedly stimulate germination and growth. He finally reached a conclusion expressed as follows: "The rays of radium act as a stimulus to protoplasm. Retardation of growth following exposure to the rays is an expression of overstimulation; acceleration of growth indicates stimulation between a minimum and an optimum point." *Gager* found that the root was more affected than the other parts of the plant, and his experiments show that members of the grass or grain family are more strongly influenced than other plants with which he experimented. He concluded that the gamma rays can penetrate as much as a foot in moist soil. As my own experiments show, they produce important effects at a distance at least seven or eight times as great as this.

In France, *Petit* and *Ancelin* reported that by placing the seeds between sheets of blotting paper moistened with radioactive water, not only were a much larger number of ray-grass seeds germinated than when plain water was used, but also the roots at the end of the thirteenth day were ten times as long as the roots of the control seeds. With wheat and corn the increased length was not so great, but was very marked, as was also the greater length of the stems.

The National Agricultural School at Grignon, France, experimented with six varieties of potatoes and obtained by the use of radium an average gain of more than 16 per cent. in the weight of the crop, the potatoes at the same time containing more starch and being correspondingly more mealy and palatable. Barley so treated gave 17.6 per cent. more straw and 12.5 per cent. more grain. Mustard gave 27 per cent. more straw and 34 per cent. more seed. Flax gave 24 per cent. more straw and 6 per cent. more seed. White vetch gave 19 per cent. and fenugreek 11.5 per cent. more fodder.

At the Agricultural School of Berthonval, the experiments were made on plots of a hectare (2.47 acres) each. Upwards of a 15 per cent. increase in the yield of grain was obtained by the radium treatment and over 14 per cent. in that of sugar beats.

At the Harper-Adams Agricultural College at Newport, *Foulkes* also obtained a 14 per cent. increase in the yield of table

beets and more than 20 per cent. in turnips, plots of a hectare each being employed.

Messrs. *Vilmorin, Andrieux* & Co. and others experimented with flowers, obtaining very satisfactory results on chrysanthemums, roses, and other cut flowers.

All experimenters with plants in pots have reported phenomenal increases in root development so that the plants quickly became root-bound and had to be successively transplanted to larger pots.

A most extensive series of experiments has been carried on at Joachimstal by Dr. Julius *Stocklasa,* Director of the Chem.-Phys. Institute at Prague, with the co-operation of four assistants. These experiments extended over a period of seven years, the results being embodied in a voluminous report, made in September, 1913. There were many series of experiments. In one set, the plants were grown in ordinary soil and watered with water possessing various degrees of radio-activity due to radium emanation. In another set they were grown in water supplied with plant food similarly charged, while in another set radioactive earth was employed. The following results were obtained:

The first experiments were directed towards ascertaining the effects of radium emanation upon the activity of those bacteria which take nitrogen from the atmosphere and fix it in the soil in the form of plant food, thus enriching the soil. He found that liquids containing these bacteria gained from 32 per cent. to 76 per cent. more plant food in this way under radioactive influence than without it. Unused soil gained from 10 per cent. to 30 per cent. more fertility in a few months from this cause under the same conditions than without the radium emanation.

Many experimenters had reported that radium exerted a toxic action on plant life, while others had declared to the contrary. *Stocklasa* repeated all these experiments, but in two series, one with very small amounts, the other with large amounts of the radium. He found that in most of the latter cases the effects were toxic, while in the former they were healthfully stimulating. He also found that different plants differed so materially in their susceptibility that the same amount of radium might be stimulant to one but toxic to another. What was even more interesting and important, he showed that families of plants manifested this difference.

When a very low radioactivity was employed, the germinating of seeds was increased from 70 per cent. to 130 per cent., but it was retarded by a high activity. Drying and weighing two sets of plants after 48 days of growth, one set under radioactivity, the other not, the former showed an increase of over 200 per cent. in peas, over 100 per cent. in beans and lupines and nearly 900 per cent. in barley. In another set of experiments, with lentils, peas and wheat, the gain by the use of radium ranged from 62 per cent. to 158 per cent. With buckwheat, the increase ran from 42 per cent. to 106 per cent. With poppies, there was an increase of 117 per cent. in the seed, and 32 per cent. in the plant exclusive of the seed, or 50 per cent. in total. With lupines the

seeds gained 64 per cent., the total gain being 60 per cent. The greatest gain was in the early stages of growth, the ratio decreasing thereafter.

These studies taught that all the main functions of the living cell are greatly stimulated by radium. The fact that starch production went on in darkness, and other corroborative facts, indicated that the effects of the radium closely resemble those of the ultra-violet rays of the sun.

He summarizes as follows:

"All our researches point to the fact that radium emanations with a low activity favorably influence the karyokinesis of the cell, the entire development of the plant, the mechanism of the metabolism, the photochemical assimilation in the chlorenchyma, bud formation and finally fructification. Too great a concentration of emanation exerts an inhibiting influence on the growth of the plant and causes toxic symptoms in the cells, both in those containing chlorophyll and those free of this substance."

He also says that if we assume that under ordinary conditions land will produce 200 cwts. per hectare of corn or cattle turnips, we may expect 300 to 400 cwts. under the influence of radium.

He concludes, finally, that the effects of radioactivity are greatest on young foliage and almost equally great on the petal tissues of the flower.

Against this array of positive evidence as to the stimulating effects of the radium, I had the negative effect of a caution from the French Agricultural Bureau against the probability of such a pronounced action as has been reported, on the ground that the amounts of radium employed were so very small. Little weight could be given to this suggestion, because of its purely speculative character. However, the case was one that called pre-eminently for the actual test of experimentation and to this I applied myself in the most practical possible way.

I made it my business for the time being, to ignore all theoretical considerations and to proceed with my trials precisely as a farmer would proceed in preparing the land and applying the radium for a market crop.

(To be concluded in the next number.)

Recent American Contributions to Radium Therapy, III.

Thomas *Ordway,* M. D., (Boston). The Use of Radium in Cancer and Allied Conditions at the Huntington Hospital—Illustrative Cases. Boston Medical and Surgical Journal, Vol. 171, pp. 771-783, Nov. 19, 1914. A paper presented in the Section of Surgery of the Massachusetts Medical Society in the Symposium on Cancer of Certain Pelvic Organs, June 9, 1914. This paper by Dr. *Ordway* is the first comprehensive statement of the results which have been obtained in the past year by the Cancer Commis-

sion of Harvard University in their investigation of the clinical value of radium in the treatment of cancer and allied conditions. The importance of such work in determining the place of radium in therapy is very great and in the following extensive quotations are made from Dr. *Ordway's* paper. The paper is illustrated with reproductions of photographs which show certain details of the applications of the radioactive material, and the results achieved.

"Up to the present time about two hundred cases have been treated. This number is insufficient and the time elapsed is too short for a comprehensive, critical report on the value of radium therapy. This paper should be regarded, therefore, in the light of a preliminary communication indicating the nature of the cases treated and showing progress in the accumulation of data for record and subsequent critical review and analysis."

"Such a clinical investigation has necessitated the combined efforts of almost the entire staff of the commission. Professor E. E. *Tyzzer*, director, has had general charge of the work and has made the pathological study of cases as far as practicable. Dr. Thomas *Ordway*, physician in charge, has prescribed the radium treatments and had immediate supervision of all the cases. Professor William *Duane*, to whom the Commission is indebted for the new methods of application, has been engaged together with his assistant, Dr. W. T. *Bovie*, in the preparations of new forms of applicators and in the measurement of their activity. Dr. Ellis *Kellert*, house physician, has taken most of the photographs and assisted in the clinical work. Dr. R. B. *Greenough*, consulting surgeon, has examined many of the patients in order to decide whether operation was advisable. From this it will be seen that many have co-operated in the work and it is as a representative of the Commission rather than its sole author that I present this preliminary announcement of progress in radium therapy at the Huntington Hospital."

"Most of the cases were of inoperable and recurrent cancer, any many of these had widespread dissemination and were in the cachectic terminal stage. A few patients having superficial lesions which were operable were treated, for cosmetic effect, at the request of their physician or the consultants above referred to. A few cases were treated after operation, in prophylaxis of recurrence. Radium treatment has not been used in cases where operation was possible and offered a reasonable hope of cure, with the exception of those superficial lesions where delay was of no consequence."

"The nature of the pathological conditions was varied and included papilloma, keratosis, verruca, leukoplakia, superficial and deep rodent ulcers, leukemia, Hodgkin's disease, so-called basal cell type of carcinoma, sarcoma—round, spindle cell and melanotic, carcinoma—epidermoid adeno and alveolar in type. Many parts of the body were affected in the different cases, notably the eye, ear, cheek, nose and mouth, tongue, jaw, neck, larynx, esophagus, breast, abdominal wall, peritoneum, ovary, uterus, rectum, and extremities."

"The methods used were those devised and already described by Dr. *Duane.*"

"The strength of a radium salt depends on the amount of radium element present. Therefore, in reporting cases the dosage should be accurately stated in milligrams of radium metal or millicuries of radium emanation per hour per unit area. A millicurie is the quantity of emanation that furnishes the same penetrating radiation that one milligram of radium element produces."

"The dose employed has varied from 10 to 75 millicuries applied for various periods of time and over areas of greater or less extent, the small dose in superficial skin lesions and the larger particularly in uterine cases. The Commission at present has 250 milligrams of radium expressed as metal."

"Tubes and surface applicators are used on patients according to the following general rules, to which, however, there are exceptions in special cases. These rules indicate only single applications and give no idea of the number or the time elapsing between them. The number varies greatly with the variety and size of the growth and the intervals in most instances are from three to six weeks, although in certain cases applications are made every day or two for a week and repeated at the regular three to six weeks' interval. The time of application depends not only on the strength of the applicators, usually from 10 to 75 millicuries, but also on the size and nature of the growth, the area to be covered, and the sensitiveness of the patient's skin."

"1. For effects upon growths beneath the skin when the latter is intact. Surface applicator—Screening 2 mm. of lead. Protection, gauze, paper and rubber. Exposure, 4 to 8 hours or less."

"2. For superficial skin lesion, such as keratosis, small growths, etc. Screening, none or 1-10 to 5-10 mm. of lead. Protection, rubber over lesion, adjacent normal skin carefully protected by shield of 1 to 2 mm. of lead, gauze and rubber. Exposure, 10 minutes to 2 hours."

"3. For deep skin lesions with ulcerations (a) Screening, none except rubber. Protection of adjacent tissues as in No. 2. Exposure, 2 to 4 hours. (b) If lesion is still deeper, screening 1 to 2 mm. of lead and rubber; exposure, 4 to 12 hours."

"4. Lesions of mucous membranes when superficial. Same as No. 2, except exposure of 1 to 2 hours."

"5. Lesions of mucous membranes when deep and growths beneath the mucous membrane. The same as No. 3, except exposure, 12 to 24, and occasionally 48 hours' duration."

"6. For introduction of radium within growths. (a) Tubes. Screening ½ to 1 mm. of silver. Protection, none. Exposure, 4 to 48 hours, depending on size and nature of the tumor. Average, 12 to 24 hours. (b) For local destructive effect. Thin steel tubes without additional filtration 1 to 2 hours up to 12 hours; length of time depending on size of the growth and the reaction desired."

"Illustrative cases only will be reported in abstract, arranged in three groups: I, That in which radium therapy may be of curative value. II, Another in which it has proved of little or no value. III, In which palliative results with particular reference

to improvement in the local or general condition were obtained."

In the following only the results obtained by radium treatment are given.

GROUP I. CASES IN WHICH RADIUM THERAPY MAY BE OF CURATIVE VALUE.

Case. 1. Rodent ulcer on left cheek below eye, 3 X 1.7 cm. Apparent cure.

Case 2. Epidermoid carcinoma on outer portion of left upper eye lid. "Note: To excise the whole area would mean sacrificing considerable portion of the lid and thus expose the eye ball to trauma of dust and possible secondary conjunctivities and sequelae. It was therefore decided to try radium therapy and operate if the condition was not relieved." Result—apparent cure.

Case 3. Adeno-carcinoma of breast—of ten years incidence, in man of 64. Ulcerated area measuring 15.5 X 11.5 cm. Result of radium treatment is considerable reduction of ulcerated area, and apparent healing going on.

Case 4. Basal cell carcinoma in temporal region of man of 68, growth about 4 cm. in diameter and 1 to 1.5 cm. in height above surrounding skin. Result of radium treatment—which is still in progress—marked diminution in size, almost disappearance of the growth.

Case 5. Epithelioma on nose recurring after operation in a woman of 73. Result of radium treatment—apparent cure.

Case 6. Epidermoid carcinoma of face—post-operative radium treatment—improved.

Case 7. Post-operative recurrence in adeno-carcinoma of the uterus—improved by radium treatment.

Case 8. Osteochondro-sarcoma of cheek near nose, treated with radium after six operations. Small recurrence. Radium treatment continued intensively.

GROUP II. CASES IN WHICH RADIUM THERAPY PROVED OF LITTLE OR NO VALUE.

Case 1. Leukoplakia. No improvement.

Case 2. Carcinoma of larynx, no determinable effect upon the growth.

Case 3. Carcinoma of the neck. No improvement.

Case 4. Carcinoma of the neck. Patient died.

Case 5. Post-operative recurrence of sarcoma of orbit. Radium treatment failed to check growth. Patient died.

Case 6. Carcinoma of breast, extensive, widespread post-operative recurrence. No subjective or objective improvement from radium treatment.

GROUP III. CASES IN WHICH PALLIATIVE RESULTS WITH PARTICULAR REFERENCE TO IMPROVEMENT IN THE LOCAL OR GENERAL CONDITION WERE OBSERVED.

Case 1. Carcinoma of the uterus, fundus, implantation metastasis in abdominal wall. Marked decrease in size of induration in abdominal wall. No improvement in general condition.

Case 2. Adeno-carcinoma of cervix with improvement in local and general condition, rendering an inoperable case operable; post-operative infection, death.

Case 3. Chronic lymphatic leukemia, marked and prompt diminution in white count and in size of spleen, relief of abdominal discomfort. Slight improvement of general condition.

Case 4. Melanotic sarcoma left nares and naso-pharynx; inoperable. Marked diminution in size of growth, which is less vascular. Improvement in breathing and hearing.

Case 5. Post-operative recurrence deep rodent ulcer. Improvement in local condition.

Case 6. Sarcoma of thigh with extension to groin and abdomen. Temporary reduction in size of growth.

Case 7. Carcinoma of larynx, temporary improvement from radium treatment, patient improving in general condition. Slight increase in the size of local growth.

Case 8. Sarcoma of frontal sinus, repeated post-operative recurrence, extension to nose, rapid retrogression under radium treatment. Marked improvement.

Case 9. Myelogenous leukemia. Marked reduction in white count and in size of spleen. Improvement in strength and general condition.

Case 10. Epithelial growth on tongue, marked diminution; practical disappearance of growth.

Case 11. Carcinoma of uterus. Post-operative recurrence following palliative amputation of cervix. Metastatic nodules in vaginal wall. Radium treatment apparently rendering the case operable. Operation. No recurrence as yet.

Case 12. Inoperable carcinoma of breast. Marked improvement in local condition.

"In considering the varying opinions regarding the results of radium therapy, it should be borne in mind that differences in dosage and technic may be, to a certain extent, responsible. Very important also is the varying resistance of different growths. It cannot always be told before treatment what cases will respond. In certain instances radium is of little or no benefit, while in others there is marked improvement as indicated by diminution in size of the growth, healng of ulceration, or alleviation of symptoms, such as pain, hemorrhage, or other discharge. Cachetic cases are apt to become 'toxic' and those with widespread metastasis are not helped by radium treatment. A few cases of cancer regarded as distinctly inoperable have, under the influence of radium therapy, become operable. In certain uterine cases, treated with radium and subsequently operated upon, infection occurred. It is possible that there is lessened resistance of the neighboring tissues to infection and a slowness in healing. Whether the radium treatment was the cause of this condition in these cases is not at present possible to state. It would seem best, however, to defer operation until at least four weeks after the radium treatment has ceased. In lymphatic and myelogenous leukemia the abnormal white cells are most markedly affected by radium applications over the spleen. The white count may become normal, the red cells and hemoglobin are increased, the spleen is reduced in size and the symptoms may be improved. Sufficient time has not elapsed to say how long these effects will continue."

"Post-operative radium therapy is extremely unsatisfactory before recurrence has taken place, for considerable damage may be done to healthy tissue, and any evidence of recurrence masked. It seems better to observe carefully the first sign of recurrence and then begin active treatment with radium whenever it is thus clearly indicated."

Conclusions. The best, apparently curative, results from radium therapy are obtained in certain types of skin and other localized forms of cancer. In myelogenous and lymphatic leukaemia the blood picture becomes almost normal, the spleen is reduced markedly in size and certain symptoms may be relieved without toxemia resulting. In many cases of true cancer which have advanced beyond the operable stage, or those recurring after operation, improvement from radium therapy may follow not only subjectively but in the local condition. This improvement may include relief from discharge, hemorrhage and pain; cleansing or healing of ulceration; diminution in size or disappearance of the growth. Such cases, however, are rarely cured. Even large growths sometimes disappear under the influence of radium, but metastasis or spreading of the growth to other parts is not prevented, or the patient may succumb to the rapid disintegration of the original growth. Newer methods may improve these results of radium therapy; at present its proved value is limited, but occasionally cases beyond these well recognized limits are distinctly benefited."

Dr. J. Louis *Ransohoff,* Inoperable Carcinoma of the Breast, Clinically Cured by Radium. The Lancet-Clinic, Vol. CXII, No. 23, Dec. 5th, 1914, p. 618. A case Reported to the Academy of Medicine of Cincinnati.

"I wish to report this case of cancer of the breast, clinically cured by radium. This case was inoperable because of a severe myocarditis and nephritis. The patient was presented at the Academy some months ago, with a scirrhus cancer in the upper outer quadrant of the left breast. We began the radium treatment in April, 1914. The tumor at that time was hard, nodular, infiltrating and about half as large as a fist. There was no palpable involvement of the axilla. She received three treatments, of twenty-four hours each, with 100 milligrams of radium, filtered through one-half millimeter brass, and one centimeter cotton, using the cross fire method."

"As you can see, there is at present absolutely no evidence of tumor in the breast. In examining this case, as in all cases of suspected tumor of the breast, it is important that examination should be made with the patient in the recumbent position, as a pendent breast can be made to simulate tumor."

In discussing the case, Dr. D. W. *Haines* said: "I think the Academy is to be congratulated upon the privilege of seeing this patient again. In March or April of this year when this patient was presented to the society, she had a distinct tumor mass in her breast possessing all the clinical characteristics of malignancy. Tonight the patient is presented without her tumor after the use

of radium. One of the most important things of malignant tumors of the breast is the clinical diagnosis. It is well, when possible, to confirm the diagnosis by laboratory methods, but this is not expedient when the non-operative plan of treatment is to be adopted. The doctor has said one thing which is very important concerning the manner of examining the breast tumors, viz., that you can always produce a tumor by compressing the breast laterally. The only way in which to obtain reliable information concerning a tumor in the breast is to place the patient on her back and palpate the breast with the palm of the hand. This method will force the tumor against the chest wall and readily detect the presence of a growth although it be but small in size."

Dr. E. G. *Zinke* added the following to the discussion: "A year ago, on my return from Chicago, a patient was waiting for me who had unmistakably carcinoma uteri with serious involvment of the adjacent structures. The anterior vaginal wall and left breast ligament was filled with a mass the size of an ordinary apple. The vaginal mass was first removed with the cautery knife. After that five applications were made with the ordinary actual cautery, i. e., the Percy method for the treatment of incurable cases of cancer of the uterus. But the growth continued to show a disposition to return within two and three weeks after every cauterization. It was about this time that Dr. *Ransohoff* secured some radium. It was tried in this case. The effect was little short of marvelous. The applications of radium have been repeated at varying intervals since that time, the last about a month ago. There has been no evidence of the return of disease for more than six months. The radium applications made of late have been prophylactic in character rather than otherwise. The result in this case has been highly gratifying. It is my opinion that radium is a valuable remedy in the hands of skilled and experienced men."

OBITUARY

Fernand L. de *Verteuil*, M.D. (Edin.) M. R. C. S. (Eng.) L. R. C. P. (Lond.) Surgeon R. N. R., of Vancouver, B. C., lost his life on the Good Hope, which was lost on Sunday, November 1st, in the naval action off the coast of Chile. Dr. de *Verteuil* was the son of Dr. J. de Verteuil, surgeon major in the British army. He was born in Trinidad in 1879 and received his medical education at Edinburgh and Paris. Dr. de *Verteuil* was particularly interested in the study of radium therapy and had written several important papers on the subject. He had been in practice in Vancouver for two years and a half. A few months ago he went to the West Indies in order to study the curative effects of radium in leprosy; while there he was ordered to join the Good Hope in the capacity of surgeon. Dr. de *Verteuil* leaves a widow and two children.

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